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Transposable elements and Chk2 mutation drive heritable germline variation in *Drosophila*

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Activation of mobile genetic elements, collectively called as transposable elements (TEs), can lead to genetic and phenotypic changes in living organisms. Animal germline has evolved gonad-specific PIWI-interacting RNAs (piRNAs) pathway to protect genome integrity against aberrant activation of TEs, resulting in global DNA double strand breaks. A critical component of this pathway is Heterochromatin Protein 1d (HP1d), or Rhino, which supports the heterochromatin-dependent transcription of piRNA precursors. In *Drosophila*, females lacking Rhino are completely sterile, while males remain fertility for a week due to gradual loss of germline stem cells (GSCs), even though TEs are strongly de-repressed. Intriguingly, the programmed cell death (cleaved caspase-3, LysoTracker and TUNEL) was barely detectable in GSCs of male *rhino* mutant, indicating the gradual loss of GSCs unlikely linked to cell death due to accumulation of DNA damage. Instead, the expression of Stat92E—an essential factor for maintaining male germline stem cells (GSCs)—was significantly reduced, implying that the observed male sterility of *rhino* mutant likely results from impaired self-renewal of GSCs. Interestingly, the sterile phenotype in male *rhino* mutants is fully rescued by addition of mutation for Checkpoint kinase 2 (Chk2, *mnk*), a kinase for DNA damage response pathway. *rhino chk2* double mutants restore the level of Stat92E in GSCs, indicating that Chk2 activated by TE de-repression disrupts Stat92E stability. These observations suggest that the activation of TEs can interfere with crucial signaling pathways like JAK/STAT. To explore the further biological implications, we observed 200 progeny lines established from individual sperm which has disrupted DNA due to de-repressed TEs. Out of them, about 10% exhibited heritable developmental abnormalities not seen in the parent generation. These findings imply that TE activity, when coupled with Chk2-mediated signaling disruption, can drive novel heritable variation in the germline.